IN THE CLAIMS

Please cancel the original slate containing claims 1-47 and add new claims 48-103 as follows:

48. A method of treating a patient suffering from poisoning or at risk of poisoning by a clostridial toxin comprising the step of supplying a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor) to a cell of the patient, wherein the SNARE is resistant to proteolysis by the said clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the elostridial toxin (toxin-inhibitory SNARE).

49. A method comprising the step of using a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor), or a recombinant polynucleotide capable of expressing the said SNARE in the manufacture of a medicament for the treatment of a patient suffering from poisoning or at risk of poisoning by a clostridial toxin, wherein the SNARE is resistant to proteolysis by the said clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the clostridial toxin (toxin-inhibitory SNARE).

50. A method of reversing the inhibition of exocytosis in a cell caused by contact of a clostridial toxin with the said cell, including the step of supplying a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor) to the said cell not before contact of the said clostridial toxin with the said cell, wherein the SNARE is resistant to proteolysis by the said clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the clostridial toxin (toxin-inhibitory SNARE).

51. A method as in any one of claims 48-50 wherein the said SNARE that is resistant to proteolysis by the said clostridial toxin is selected from the group consisting of synaptosomal-associated polypeptide of 25 kDA (SNAP-25), syntaxen 1 and synaptobrevin that is resistant to proteolysis by the said clostridial toxin.

52. A method as in any one of claims 48-50 wherein the SNARE that is capable of inhibiting the clostridial toxin (toxin-inhibitory SNARE) is selected from the group consisting of synaptosomal-associated polypeptide of 25 kDA (SNAP-25) that is capable of inhibiting the clostridial toxin and a SNARE in which the residue immediately N-terminal to the clostridial toxin cleavage site is replaced by a cysteine residue.

53. A method as in any one of claims 48-50 wherein the said clostridial toxin is botulinum toxin A (BoNT/A).

54. A method as in claim 51 wherein the said clostridial toxin is botulinum toxin A (BoNT/A).

55. A method as in claim 52 wherein the said clostridial toxin is botulinum toxin A (BoNT/A).

56. A method as in claim 51 wherein the said SNARE is resistant to proteolysis by botulinum toxins A, B and Cl (BoNT/A, BoNT/B and BoNT/C1).

57. A method as in claim 54 wherein the said SNARE is a variant of SNAP-25 in which the residue equivalent to residue 197 and/or the residue equivalent to residue 198 of full length SNAP-25 are replaced by a residue other than Q or a residue other than R, respectively.

58. A method as in claim 57 wherein the said SNARE is a variant of SNAP-25 in which the residue equivalent to residue 197 and/or the residue equivalent to residue 198 of full length SNAP-25 are replaced by a residue other than Q or a residue other than R, respectively.

59. A method as in claim 57 wherein the residue equivalent to R198 of full length human SNAP-25 is replaced by a residue other than R, selected from A, T, K, H or W and the residue equivalent to residue Q197 of full length SNAP-25 is Q or is replaced, by A, K or W.

60. A method as in claim 58 wherein the residue equivalent to R198 of full length human SNAP-25 is replaced by a residue other than R, selected from A, T, K, H or W and the residue equivalent to residue Q197 of full length SNAP-25 is Q or is replaced, by A, K or W.

61. A method as in any one of claims 48-50 wherein the said SNARE that is resistant to proteolysis by the said clostridial toxin is capable of performing substantially the equivalent function to a SNARE present in the cell that is capable of being cleaved in the said cell by the said clostridial toxin.

62. A method as in claim 51 wherein the said SNARE that is resistant to proteolysis by the said clostridial toxin is capable of performing substantially the equivalent function to a SNARE present in the cell that is capable of being cleaved in the said cell by the said clostridial toxin.

63. A method as in either of claims 48 or 49 wherein the patient has or is at risk of botulism.

64. A method as in either of claims 48 or 49 wherein the patient has or is at risk of tetanus.

65. A method as in claim 51 wherein the patient has or is at risk of tetanus.

66. A method as in claim 52 wherein the patient has or is at risk of tetanus.

67. A method as in claim 61 wherein the patient has or is at risk of tetanus.

68. A method as in claim 62 wherein the patient has or is at risk of tetanus.

69. A method as in either of claims 48 or 49 wherein the patient is an infant.

70. A method as in claim 51 wherein the patient is an infant.

71. A method as in either of claims 48 or 49 further comprising the steps of determining the type of the said clostridial toxin from which the patient is suffering and of selecting an appropriate SNARE that is resistant to proteolysis by the determined clostridial toxin and/or is capable of inhibiting the determined clostridial toxin for use in the treatment.

72. A method as in claim 51 further comprising the steps of determining the type of the said elostridial toxin from which the patient is suffering and of selecting an appropriate SNARE that is resistant to proteolysis by the determined clostridial toxin and/or is capable of inhibiting the determined clostridial toxin for use in the treatment.

73. A method as in either of claims 48 or 49 further comprising the step of treating the patient with an inhibitor of the said clostridial toxin.

74. A method as in claim 51 further comprising the step of treating the patient with an inhibitor of the said clostridial toxin.

75. A method as in claim 73 wherein the inhibitor of the said clostridial toxin is a SNARE that is capable of inhibiting the said clostridial toxin (toxin-inhibitory SNARE) or a recombinant polynucleotide capable of expressing the said toxin-inhibitory SNARE.

76. A method as in claim 74 wherein the inhibitor of the said clostridial toxin is a SNARE that is capable of inhibiting the said clostridial toxin (toxin-inhibitory SNARE) or a recombinant polynucleotide capable of expressing the said toxin-inhibitory SNARE.

77. A method of treating a patient in need of inhibition of SNARE-dependent exocytosis from a cell capable of performing SNARE-dependent exocytosis comprising the step of supplying a fragment, variant, fusion or derivative of a SNARE or a fusion of a said fragment, variant or derivative (inhibitory SNARE) that is capable of inhibiting SNARE-dependent exocytosis to the said cell of the patient.

78. A method comprising the step of using an entity selected from the group consisting of (1) a fragment, variant, fusion or derivative of a SNARE or a fusion of a said fragment, variant or derivative (inhibitory SNARE) that is capable of inhibiting SNARE-dependent exocytosis or (2) a recombinant polynucleotide capable of expressing a fragment, variant, fusion or derivative of a SNARE or a fusion of a said fragment, variant or derivative (inhibitory SNARE) that is capable

of inhibiting SNARE-dependent exocytosis in the manufacture of a medicament for the treatment of a patient in need of inhibition of SNARE-dependent exocytosis from a cell capable of performing SNARE-dependent exocytosis.

79. A method as in either of claims 77 or 78 wherein said inhibitory SNARE is a fragment derivable by cleavage of a SNARE by a clostridial toxin.

80. A method as in claim 79 wherein said inhibitory SNARE is a fragment derivable by cleavage of SNAP-25 or a variant thereof by BoNT/A.

81. The method or use of claim 80 wherein said inhibitory SNARE consists of residues identical to residues 1 to 197 of full length SNAP-25 or a variant thereof.

82. A method as in either one of claims 77 or 78 wherein the cell is a nerve cell adreno-chromaffin cell or insulin-secreting cell.

83. A method as in claim 79 wherein the cell is a nerve cell adreno-chromaffin cell or insulin-secreting cell.

84. A method as in claim 80 wherein the cell is a nerve cell adreno-chromaffin cell or insulin-secreting cell.

85. A method as in claim 81 wherein the cell is a nerve cell adreno-chromaffin cell or insulin-secreting cell.

86. A pharmaceutical formulation comprising a SNARE polypeptide, toxin-resistant SNARE or inhibitory SNARE, molecule recombinant polynucleotide encoding an entity selected from the group consisting of a SNARE or a variant, fragment, derivative or fusion thereof for use in medicine together with one or more acceptable carriers.

87. A molecule which comprises an entity selected from the group consisting of a SNARE polypeptide or toxin-resistant or toxin-inhibitory SNARE polypeptide or inhibitory SNARE polypeptide and a further portion.

88. A molecule as in claim 87 wherein said further portion is capable of promoting cellular uptake of the molecule or the entity selected from the group consisting of said SNARE polypeptide or toxin-resistant or toxin-inhibitory SNARE polypeptide or inhibitory SNARE polypeptide.

89. A molecule as in either claim 87 or 88 wherein said further portion is an inactive clostridial neurotoxin having specificity for a target nerve cell.

90. A polypeptide that is a variant, fragment, derivative or fusion of SNAP-25 that is resistant to cleavage by BoNT/A or is capable of inhibiting BoNT/A wherein (1) the residue equivalent to residue Q197 of full length SNAP-25 is replaced by A or W and the said fragment is at least 18 amino acids in length or (2) the residue equivalent to residue R198 of full length SNAP-25 is replaced by H or W, and the said fragment is at least 18 amino acids in length or (3) the residue equivalent to residue Q197 of full length SNAP-25 is replaced by A, K or W and the residue equivalent to R198 of full length SNAP-25 is replaced by a residue other than R, preferably A, T, K, H or W or (4) the residue equivalent to residue R198 of full length SNAP-25 is replaced by a

residue other than R, preferably A, T, K, H or W wherein residues equivalent to one or more of amino acids 203 to 206 are not present or (5) the polypeptide is also resistant to cleavage by BoNT/E and BoNT/C or (6) the residue equivalent to residue Q197 of full length SNAP-25 is replaced by C.

91. A polypeptide consisting of residues identical to residues 1 to 198, 199, 200 or 201 of full length SNAP-25 or a variant thereof, or a fusion either thereof.

92. A SNARE in which the residue immediately N-terminal to a clostridial toxin cleavage site is replaced by a cysteine residue.

93. A SNARE as in claim 92 wherein said cleavage site is a BoNT/A cleavage site.

94. A nucleic acid encoding an entity selected from the group consisting of a polypeptide according to claim 90 or 92 or a molecule according to claim 87 or 88.

95. A nucleic acid suitable for expressing an entity selected from the group consisting of a polypeptide according to claim 90 or 91 or 92 or a molecule according to claim 48 or 49 or 50.

96. A recombinant polynucleotide encoding an entity selected from the group consisting of a SNARE or a variant, fragment, derivative or fusion thereof for use in medicine.

97. A recombinant polynucleotide or nucleic acid as claimed in claim 96 used in a gene therapy construct.

98. A gene therapy delivery system comprising an inactive clostridial neurotoxin having specificity for a target nerve cell and a polynucleotide comprising a target nerve cell-specific promoter.

99. A gene therapy delivery system as in claim 87 wherein the inactive clostridial neurotoxin has specificity for a cholinergic neuron and the target nerve cell-specific promoter is specific for a cholinergic neuron.

100. A gene therapy construct according to claim 97, further comprising an inactive clostridial neurotoxin having specificity for a target nerve cell.

101. A gene therapy construct according to claim 100 further comprising a target nerve cell-specific promoter.

102. A kit of parts comprising;

(a) means for determining the type of clostridial, preferably botulinum, toxin from which a patient is suffering or means for determining that a patient is suffering from a particular type of clostridal, preferably botulinum, toxin; and

(b) an entity selected form the group consisting of a toxin-resistant and/or toxin-inhibitory SNARE wherein the SNARE is resistant to proteolysis by clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the elostridial toxin (toxin-inhibitory SNARE) or recombinant polynucleotide capable of expressing said toxin-resistant or toxin-inhibitory SNARE.